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(54) Title: REMEDY FOR VIRAL DISEASE

(54) 発明の名称: ウイルス治療薬

(57) Abstract: It is intended to provide a medicinal composition for preventing or treating viral infection. A medicinal composition containing a compound, which has an extremely potent anti-HCV activity and an HCV amplification inhibitory effect and shows little cytotoxicity *in vivo*, is highly useful as a preventive/remedy for HCV.

(57) 要約: 本発明は、ウイルス感染症を予防または治療するための医薬組成物の提供を目的とする。本発明の化合物は、非常に強い抗ＨＣＶ活性及びＨＣＶの増幅抑制効果を有し、かつ、インビボ細胞毒性については軽微であることから、本発明の化合物を含む医薬組成物は抗ＨＣＶ予防／治療剤として極めて有用である。

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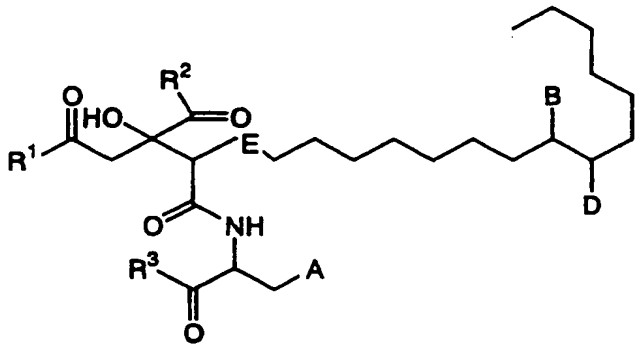
Claims

1. A pharmaceutical composition for preventing or treating viral infectious diseases comprising a compound represented by the following general formula (I):



(wherein

A represents a phenyl group substituted with -OX, or a 3-indolyl group;

X represents a hydrogen atom, a linear or branched alkyl group having 1 to 8 carbon atoms, a linear or branched alkenyl group having 2 to 8 carbon atoms, or a linear or branched alkynyl group having 2 to 8 carbon atoms;

B represents a hydrogen atom, a hydroxyl group, an oxo group, $-N(R^4)(R^5)$, $=N-OH$, $=N-OR^6$ or a halogen atom;

R^4 and R^5 may be the same or different, and each represent a hydrogen atom, a linear or branched alkyl group having 1 to 6 carbon atoms, a linear or branched alkenyl group having 2 to 6 carbon atoms, or a linear or branched alkynyl group having 2 to 6 carbon atoms, or R^4 and R^5 together represent a 3 to 8 membered ring;

R^6 represents a linear or branched alkyl group having 1 to 8 carbon atoms (which may be substituted with an amino group which may be mono- or di-substituted with a linear or branched alkyl group having 1 to 4 carbon atoms);

D represents a hydrogen atom or a hydroxyl group;

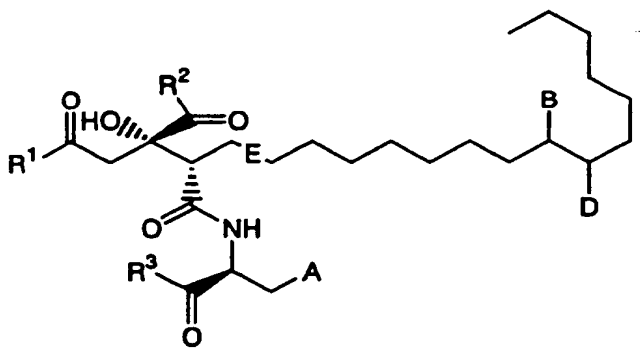
bond E represents a single bond or double bond;

R^1, R^2 and R^3 may be the same or different, and each

represent a hydrogen atom, a hydroxyl group, an amino group (which may be mono- or di-substituted with a linear or branched alkyl group having 1 to 4 carbon atoms), -OZ, a linear or branched alkyl group having 1 to 4 carbon atoms, a linear or branched alkenyl group having 2 to 4 carbon atoms, or a linear or branched alkynyl group having 2 to 4 carbon atoms; and,

Z represents a linear or branched alkyl group having 1 to 4 carbon atoms, a linear or branched alkenyl group having 2 to 4 carbon atoms, or a linear or branched alkynyl group having 2 to 4 carbon atoms)
a prodrug thereof or a pharmaceutically acceptable salt thereof.

2. The pharmaceutical composition according to claim 1 comprising the compound of formula (I) according to claim 1 represented by the following general formula (I'), a prodrug thereof or a pharmaceutically acceptable salt thereof:



(wherein A, B, D, bond E, R^1, R^2 and R^3 are the same as defined in claim 1).

3. The pharmaceutical composition according to claim 1 or 2 comprising a compound of formula (I), a prodrug thereof or a pharmaceutically acceptable salt thereof wherein A represents a phenyl group substituted with -OX at position 4, X represents a hydrogen atom, a linear or

branched alkyl group having 1 to 8 carbon atoms, a linear or branched alkenyl group having 2 to 8 carbon atoms, or a linear or branched alkynyl group having 2 to 8 carbon atoms.

4. The pharmaceutical composition according to any one of claims 1 to 3 comprising a compound of formula (I), a prodrug thereof or a pharmaceutically acceptable salt thereof, wherein B represents an oxo group, a hydrogen atom, a hydroxyl group or $=N-OR^6$.

5. The pharmaceutical composition according to any one of claims 1 to 4 comprising a compound of formula (I), a prodrug thereof or a pharmaceutically acceptable salt thereof, wherein R^1, R^2 and R^3 may be the same or different and each represent a hydroxyl group, an amino group, or -OZ (wherein Z represents a linear or branched alkyl group having 1 to 4 carbon atoms).

6. The pharmaceutical composition according to claim 1 or 2 comprising a compound of formula (I), a prodrug thereof or a pharmaceutically acceptable salt thereof, wherein A represents a phenyl group substituted with -OX at position 4, X represents a hydrogen atom, a linear or branched alkyl group having 1 to 8 carbon atoms, a linear or branched alkenyl group having 2 to 8 carbon atoms or a linear or branched alkynyl group having 2 to 8 carbon atoms, B represents an oxo group, a hydroxyl group or $=N-OR^6$, and R^1, R^2 and R^3 may be the same or different and each represent a hydroxyl group or -OZ (wherein Z represents a linear or branched alkyl group having 1 to 4 carbon atoms).

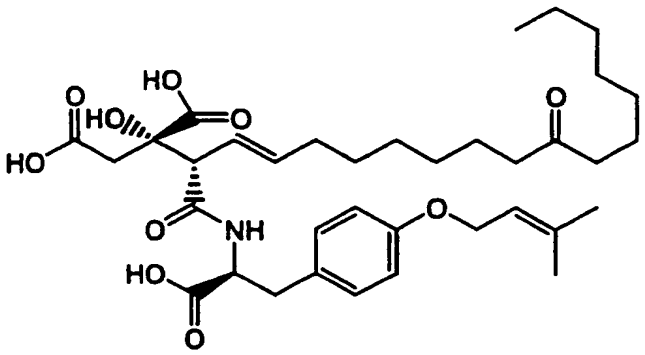
7. The pharmaceutical composition according to claim 6 comprising a compound of formula (I), a prodrug thereof or a pharmaceutically acceptable salt thereof, wherein X

represents a linear or branched alkyl group having 1 to 8 carbon atoms, a linear or branched alkenyl group having 2 to 8 carbon atoms or a linear or branched alkynyl group having 2 to 8 carbon atoms, B represents an oxo group or a hydroxyl group, and R^1, R^2 and R^3 each represent a hydroxyl group.

8. The pharmaceutical composition according to claim 1 or 2 comprising a compound of formula (I), a prodrug thereof or a pharmaceutically acceptable salt thereof, wherein A represents a 3-indolyl group.

9. The pharmaceutical composition according to claim 8 comprising a compound of formula (I), a prodrug thereof or a pharmaceutically acceptable salt thereof, wherein B represents an oxo group or a hydroxyl group, and R^1, R^2 and R^3 each represent a hydroxyl group.

10. The pharmaceutical composition according to claim 1 or 2 comprising a compound of formula (I), a prodrug thereof of a pharmaceutically acceptable salt thereof, selected from the compounds indicated below.



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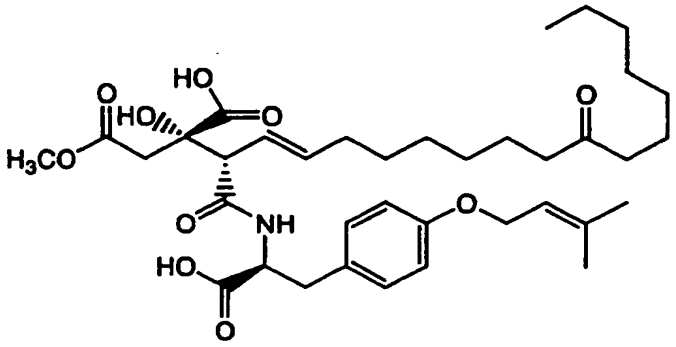

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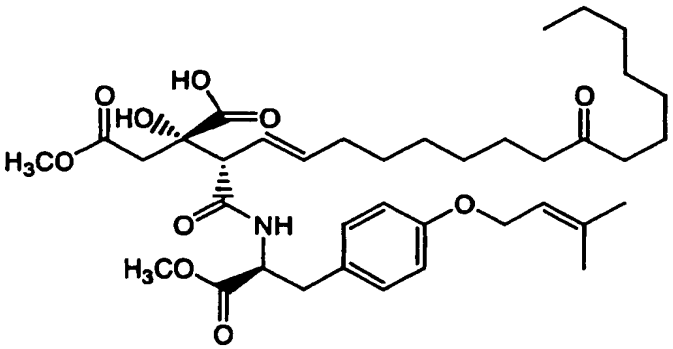

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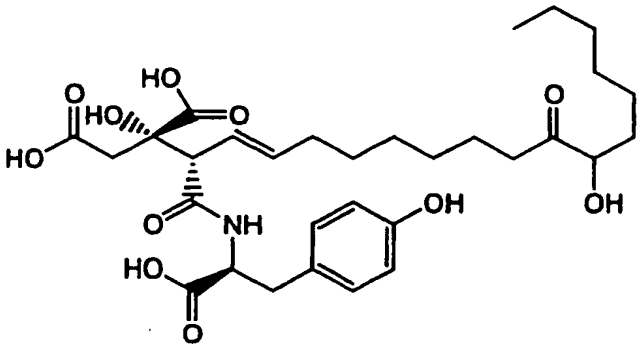

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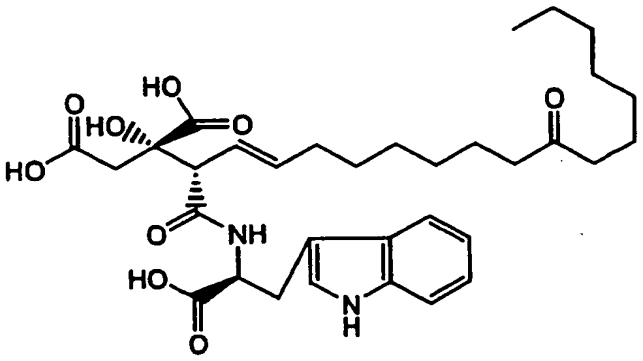

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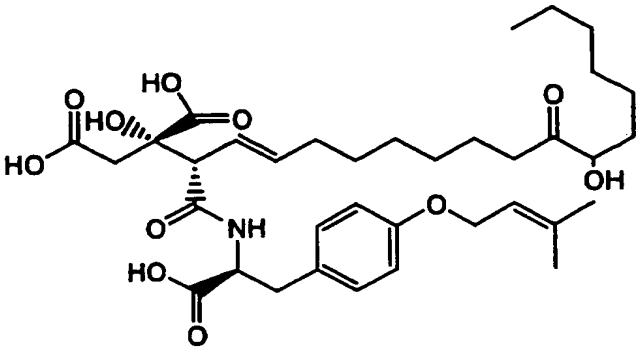

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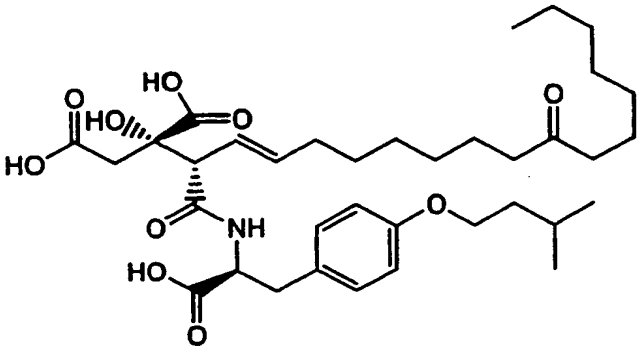

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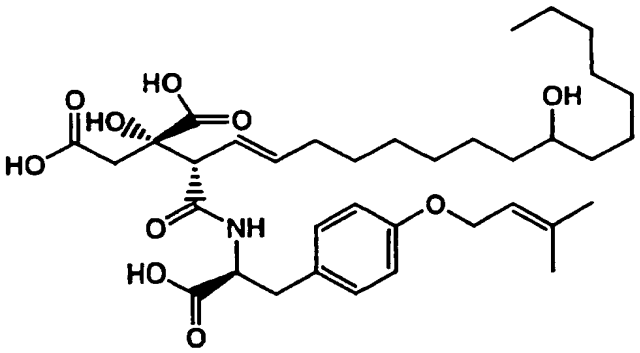

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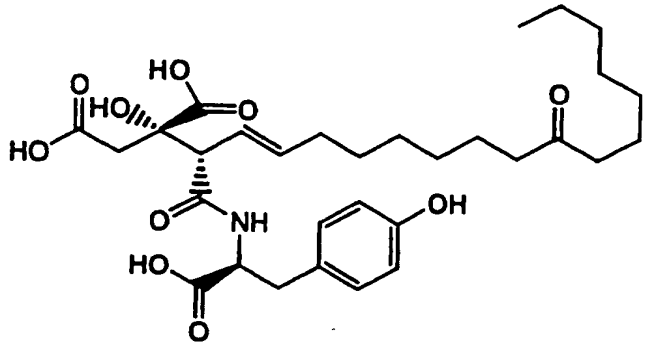

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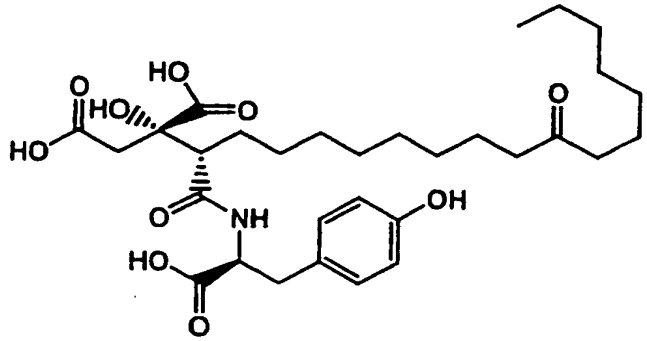

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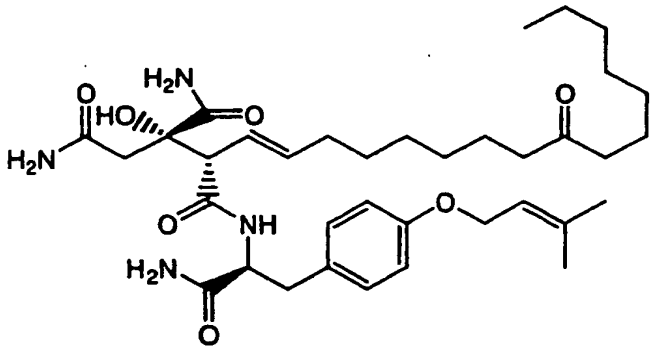

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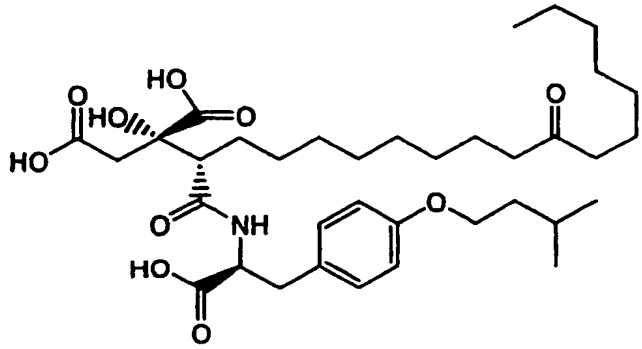

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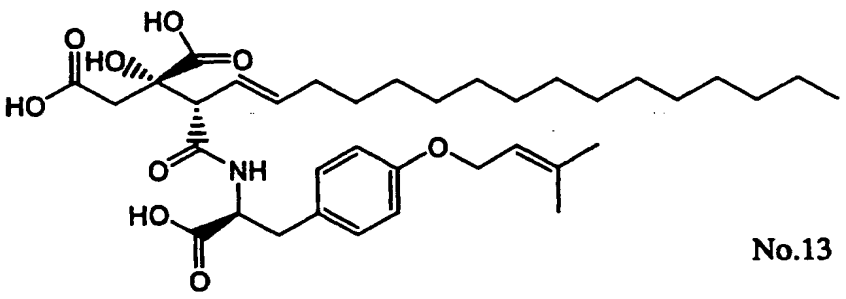

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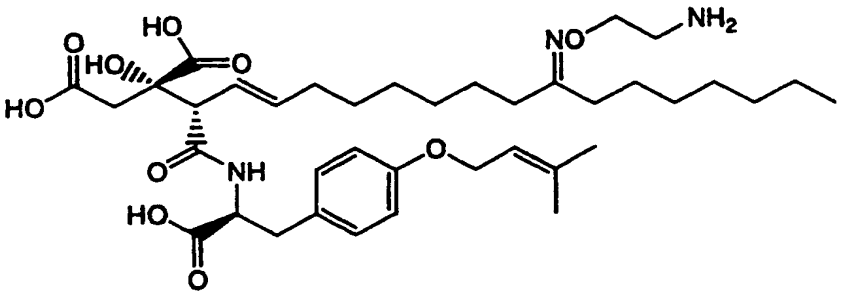
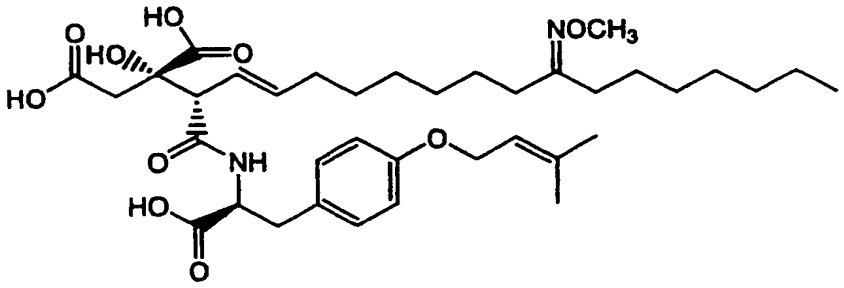


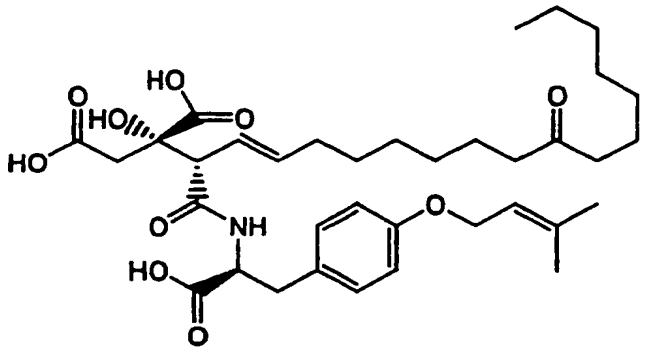
No.14

or



No.15

11. The pharmaceutical composition according to claim 1 or 2 comprising a compound of formula (I), a prodrug thereof or a pharmaceutically acceptable salt thereof, selected from the compounds indicated below.



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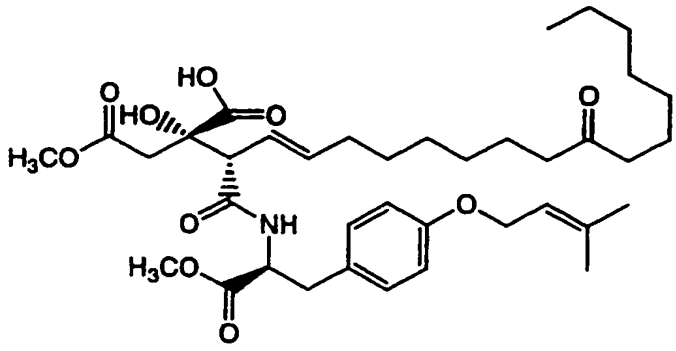

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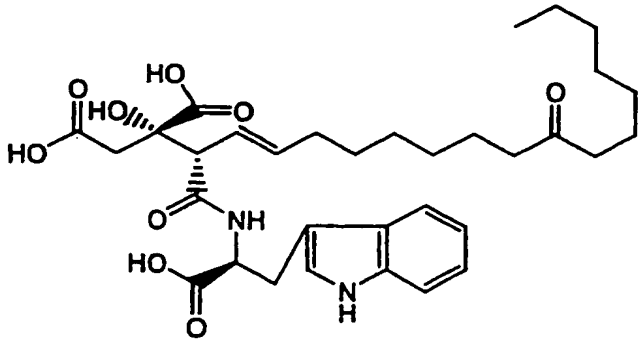

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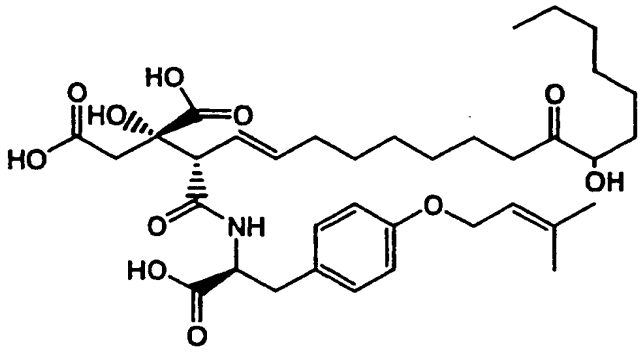

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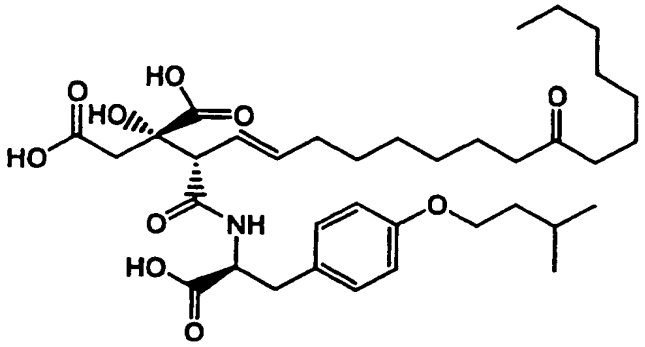

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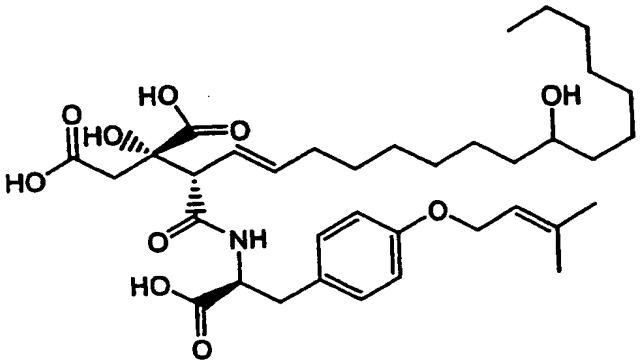

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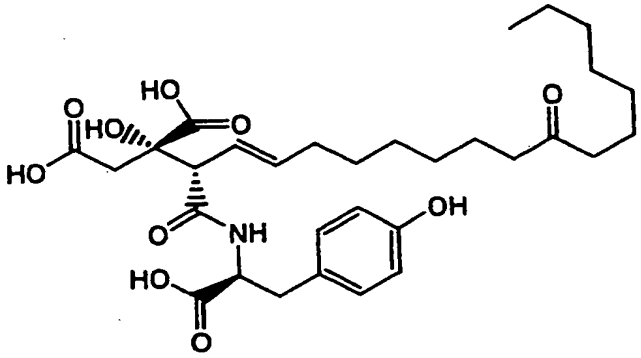

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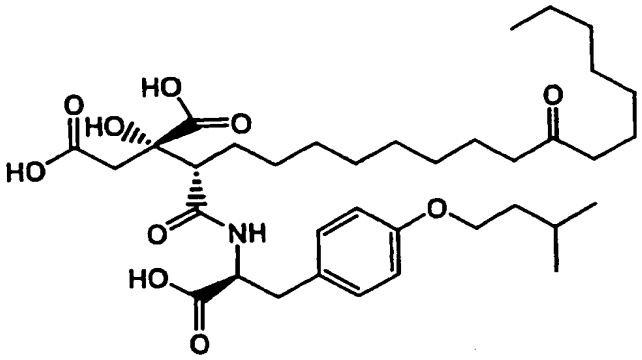

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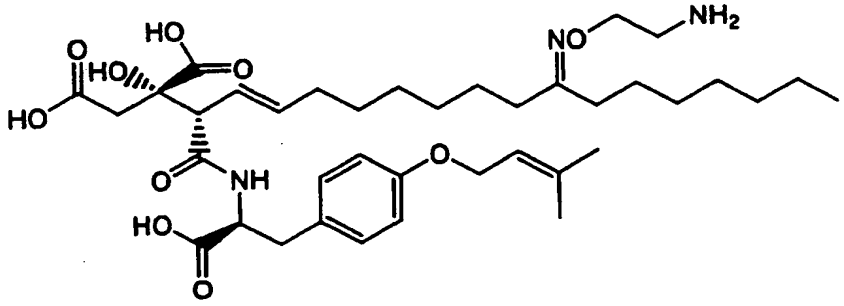

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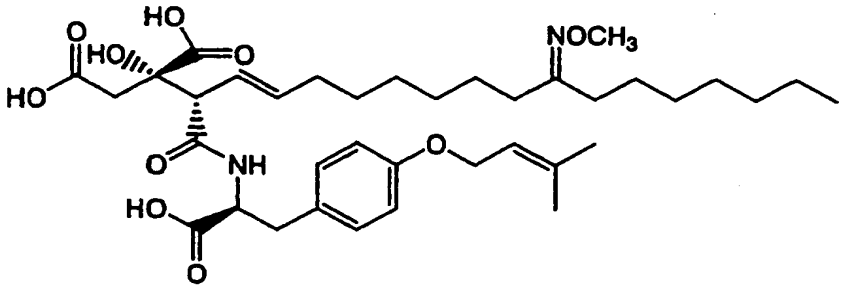
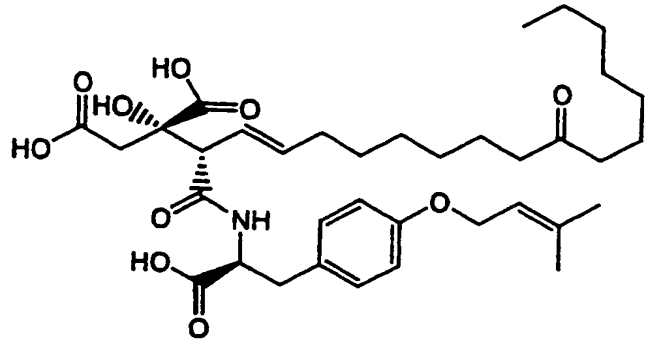


No.15

12. The pharmaceutical composition according to claim 1 or 2 comprising a compound of formula (I), a prodrug thereof or a pharmaceutically acceptable salt thereof, selected from the compounds indicated below.



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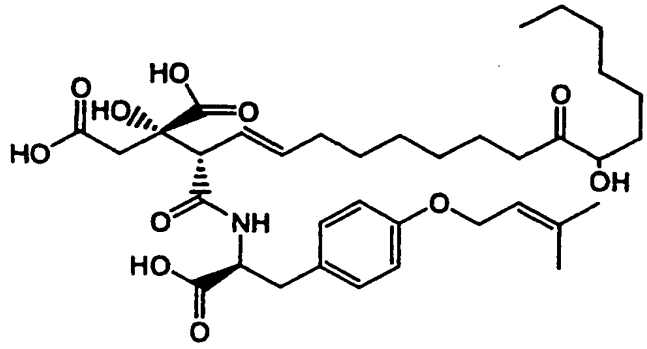

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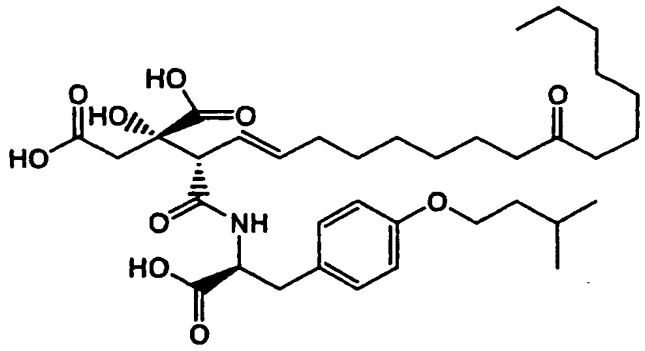

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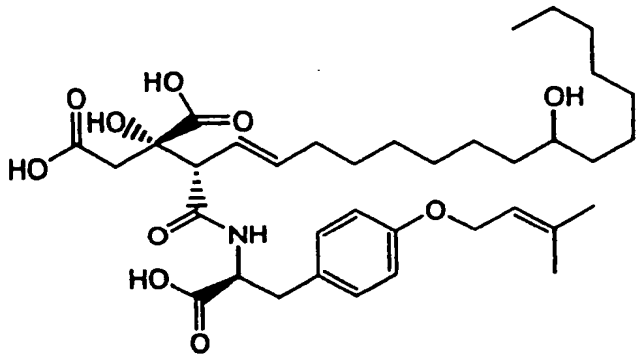
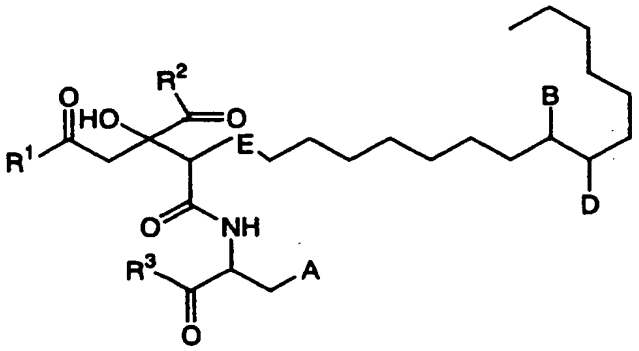


No.8

13. The pharmaceutical composition according to any one of claims 1 to 12, wherein the viral infectious disease is HCV infection.

14. The pharmaceutical composition according to claim 13, wherein the HCV infection is hepatitis C.

15. A compound represented by the following general formula (I):



(wherein

A represents a phenyl group substituted with -OX;

X represents a hydrogen atom, a linear or branched alkyl group having 1 to 8 carbon atoms, a linear or branched alkenyl group having 2 to 8 carbon atoms, or a linear or branched alkynyl group having 2 to 8 carbon atoms;

B represents a hydrogen atom, a hydroxyl group, an oxo group, $-N(R^4)(R^5)$, $=N-OH$, $=N-OR^6$ or a halogen atom;

R^4 and R^5 may be the same or different, and each represent a hydrogen atom, a linear or branched alkyl group having 1 to 6 carbon atoms, a linear or branched alkenyl group having 2 to 6 carbon atoms, or a linear or branched alkynyl group having 2 to 6 carbon atoms, or R^4 and R^5 together represent a 3 to 8 membered ring;

R^6 represents a linear or branched alkyl group having 1 to 8 carbon atoms (which may be substituted with an amino group which may be mono- or di-substituted with a linear or branched alkyl group having 1 to 4 carbon atoms);

D represents a hydrogen atom or a hydroxyl group;

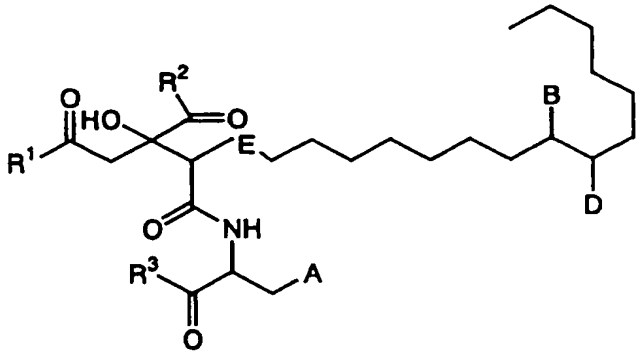
bond E represents a single bond or double bond;

R^1, R^2 and R^3 may be the same or different, and each

represent a hydrogen atom, a hydroxyl group, an amino group (which may be mono- or di-substituted with a linear or branched alkyl group having 1 to 4 carbon atoms), -OZ, a linear or branched alkyl group having 1 to 4 carbon atoms, a linear or branched alkenyl group having 2 to 4 carbon atoms, or a linear or branched alkynyl group having 2 to 4 carbon atoms; and,

Z represents a linear or branched alkyl group having 1 to 4 carbon atoms, a linear or branched alkenyl group having 2 to 4 carbon atoms, or a linear or branched alkynyl group having 2 to 4 carbon atoms, with the proviso that the case in which A is a phenyl group substituted with -OX at the p position, X is a 2-isopentenyl group or a hydrogen atom, B is an oxo group, D is a hydrogen atom, E represents a double bond, and all of R^1 to R^3 are a hydroxyl group, and the case in which A is a phenyl group substituted with -OX at position p, X is a 2-isopentenyl group, B is an oxo group, D is a hydrogen atom, bond E represents a double bond, and all of R^1 to R^3 are a methoxy group are excluded)
a prodrug thereof or a pharmaceutically acceptable salt thereof.

16. A compound represented by the following general formula (I):



(wherein

A represents a phenyl group substituted with -OX;

X represents a hydrogen atom, a linear or branched

alkyl group having 1 to 8 carbon atoms, a linear or branched alkenyl group having 2 to 8 carbon atoms, or a linear or branched alkynyl group having 2 to 8 carbon atoms;

B represents a hydrogen atom, a hydroxyl group, an oxo group, $-N(R^4)(R^5)$, $=N-OH$, $=N-OR^6$ or a halogen atom;

R^4 and R^5 may be the same or different, and each represent a hydrogen atom, a linear or branched alkyl group having 1 to 6 carbon atoms, a linear or branched alkenyl group having 2 to 6 carbon atoms, or a linear or branched alkynyl group having 2 to 6 carbon atoms, or R^4 and R^5 together represent a 3 to 8 membered ring;

R^6 represents a linear or branched alkyl group having 1 to 8 carbon atoms (which may be substituted with an amino group which may be mono- or di-substituted with a linear or branched alkyl group having 1 to 4 carbon atoms);

D represents a hydrogen atom or a hydroxyl group;

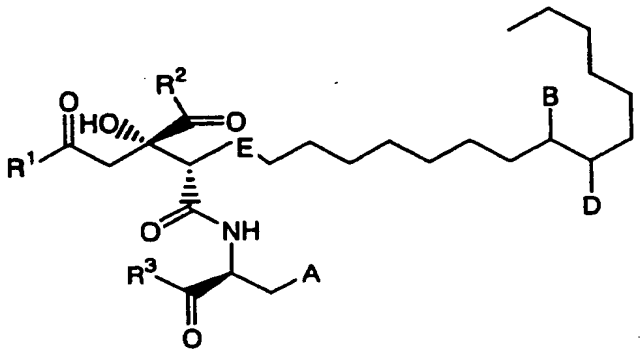
bond E represents a single bond or double bond;

R^1, R^2 and R^3 may be the same or different, and each represent a hydrogen atom, a hydroxyl group, an amino group (which may be mono- or di-substituted with a linear or branched alkyl group having 1 to 4 carbon atoms), -OZ, a linear or branched alkyl group having 1 to 4 carbon atoms, a linear or branched alkenyl group having 2 to 4 carbon atoms, or a linear or branched alkynyl group having 2 to 4 carbon atoms; and,

Z represents a linear or branched alkyl group having 1 to 4 carbon atoms, a linear or branched alkenyl group having 2 to 4 carbon atoms, or a linear or branched alkynyl group having 2 to 4 carbon atoms, with the proviso that the case in which A is a phenyl group substituted with -OX at position p and X is a hydrogen atom, and the case in which A is a phenyl group substituted with -OX at position p, X is a 2-isopentenyl group, B is an oxo group, D is a hydrogen atom, bond E indicates a double bond, and

all of R^1 to R^3 are a hydroxyl group or a methoxy group are excluded)
a prodrug thereof or a pharmaceutically acceptable salt thereof.

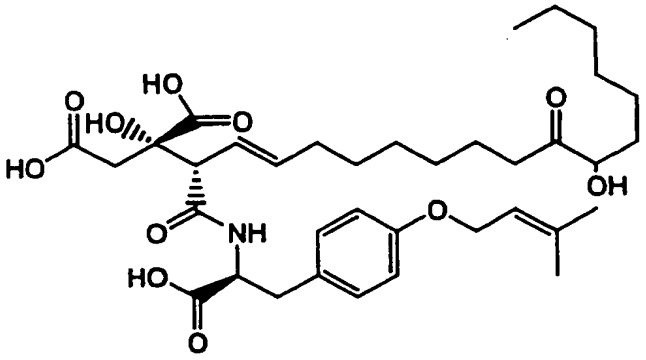
17. The compound of formula (I) according to claim 15 or 16 represented by the following general formula (I'), a prodrug thereof or a pharmaceutically acceptable salt thereof:



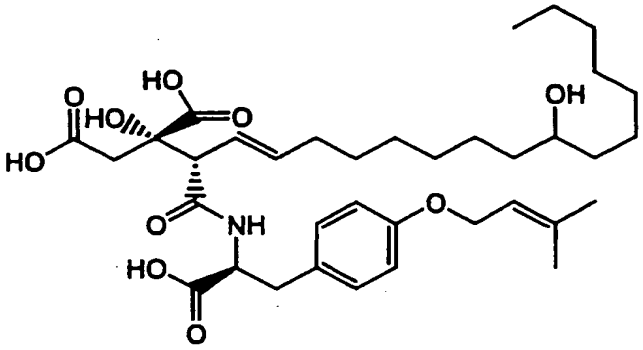
(wherein X, B, D, bond E, R^1, R^2 and R^3 are the same as described in claim 15).

18. The compound of formula (I) according to claims 15 to 17, a prodrug thereof or a pharmaceutically acceptable salt thereof, wherein X represents a linear or branched alkyl group having 1 to 8 carbon atoms, a linear or branched alkenyl group having 2 to 8 carbon atoms or a linear or branched alkynyl group having 2 to 8 carbon atoms, and B represents a hydroxyl group, an oxo group or $=N-OR^6$.

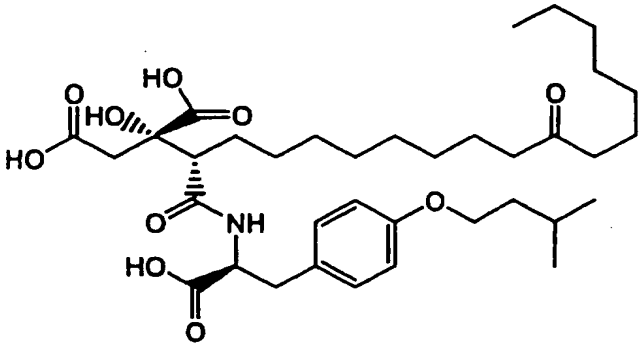
19. The compound of formula (I) according to any one of claims 15 to 18 represented by the following formula, a prodrug thereof or a pharmaceutically acceptable salt thereof.



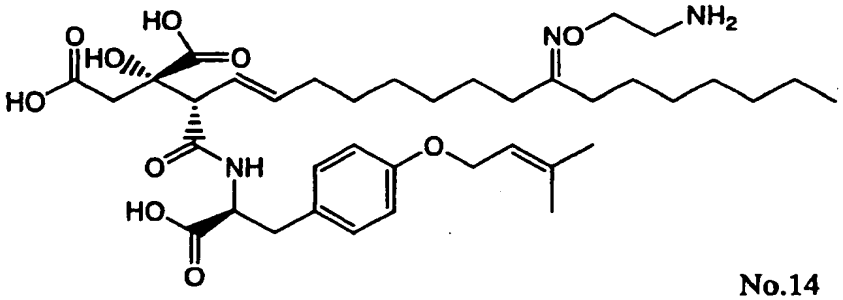
No.6



No.8

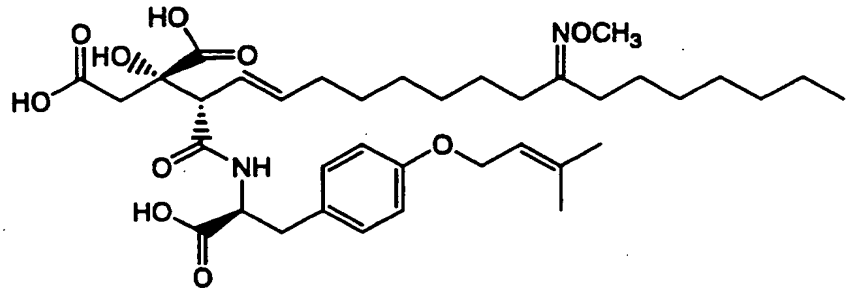


No.12



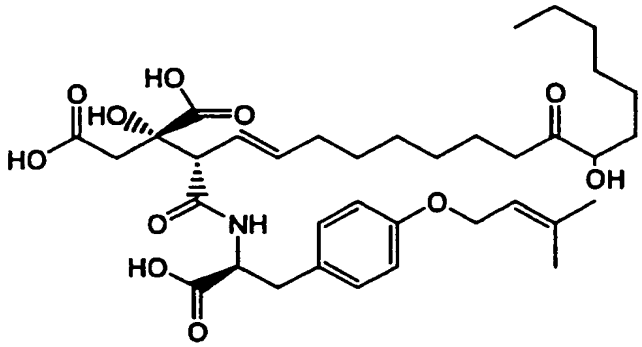
No.14

or



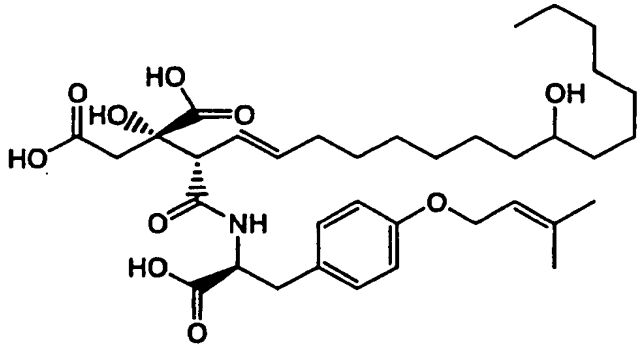
No.15

20. The compound of formula (I) according to any one of claims 15 to 18 represented by the following formula, a prodrug thereof or a pharmaceutically acceptable salt thereof.



No.6

or



No.8

21. A pharmaceutical composition comprising a compound of formula (I) according to any one of claims 15 to 20, a prodrug thereof or a pharmaceutically acceptable salt thereof.

22. The pharmaceutical composition according to claim

21 for preventing or treating of viral infectious diseases.

23. The pharmaceutical composition according to claim 22, wherein the viral infectious disease is HCV infection.

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24. The pharmaceutical composition according to claim 23, wherein the HCV infection is hepatitis C.